

II. AMENDMENTS TO THE CLAIMS

Immediately following is a complete listing of all claims, with approved status identifiers.

1. (Canceled) A cellular composition, comprising cells isolated from a poorly differentiated uterine cancer.
2. (Canceled) A cellular composition as described in claim 1 hereinabove, wherein said cancer comprises endometrial cancer.
3. (Canceled) A cellular composition as described in claim 1 hereinabove, wherein said cancer comprises adenocarcinoma.
4. (Canceled) A cellular composition as described in claim 1 hereinabove, said cancer having characteristics consistent with a primary tumor.
5. (Canceled) A cellular composition as described in claim 1 hereinabove, wherein said cancer is metastatic.
6. (Canceled) A cell line as described in claim 1 hereinabove, wherein a plurality of said cells have at least 48 chromosomes.
7. (Canceled) A cell line as described in claim 1 hereinabove, wherein a plurality of said cells are at least triploid at chromosomes 3, 7 and 17, but only haploid at chromosome 14.
8. (Canceled) A cellular composition described in claim 1 hereinabove, wherein said cells are

grown *in vitro* as a monolayer.

9. (Canceled) A human endometrial adenocarcinoma cell line described in claim 1 hereinabove, wherein a plurality of said cells have at least the following karyotypic characteristics: 48, XX, ?t (1:20) (p?34.3; p11.2), dup (2) (q11.1q23), +3, del (5) (q?23q?31), ?add(6) (p23), add (7) (p?21), +add (7) (q22), der(9;14) (q10;q10), add (15) (p11), +der (17) t(17,;19) (p11.1;p11.1), I (19) (q10), ?del (20) (p?11.2).

10. (Canceled) A line of cells originating from a specimen of human endometrial adenocarcinoma wherein a plurality of said cells behaves in substantially equivalent ways at the morphological, physiological or molecular levels as a cell of said sample.

11. (Canceled) A method of culturing cells *in vitro*, comprising the steps introducing said cells to media comprising a 1:1 mixture of Medium 199 and Ham's F12 supplemented with up to 4% serum, antibiotics, anti-micotics and growth factors; and culturing said cells under conditions for proliferation.

12. (Canceled) A method of culturing cells described in claim 11 hereinabove, comprising the steps of:

suspending cells, separated from a specimen cancer tissue, in a digestion media including (comprising) a mixture of collagenase A in a growth media comprising Medium 199 and Ham's F12 supplemented with fetal bovine serum, bovine calf serum, penicillin streptomycin, L-glutamine, fungizone and insulin transferrin selenium,

centrifuging said suspension until pellet formation,

introducing said pellet to a growth media including media comprising Medium 199 and Ham's F12 supplemented with fetal bovine serum, bovine calf serum, penicillin streptomycin, L-glutamine, fungizone and insulin transferrin selenium,
centrifuging said introductory solution, and
plating a supernatant onto a plating dish including culture media comprising Medium 199 and Ham's F12 supplemented with fetal bovine serum, bovine calf serum, penicillin streptomycin, L-glutamine, fungizone and insulin transferrin selenium.

13. (Canceled) A method of culturing a cell line described in claim 1 hereinabove, comprising the steps of:

obtaining a hysterectomy specimen of endometrial adenocarcinoma, and placing said specimen in media 1 including Leibovitz L-15 media, 5% penicillin/streptomycin, 500 µg/ml gentamicin and 2.5 µg/ml fungizone;

washing said specimen with Hank's Balanced Salt Solution ("HBSS");

mincing said specimen into 1 mm pieces, with sterile blades;

washing said pieces with HBSS;

centrifuging said pieces for 3 minutes at 700 rpm, until pellet formation;

exposing said pellet to 2 µg/ml of collagenase A in growth media 2 comprising a 1:1 mixture of Medium 199 and Ham's F12 supplemented with 1% fetal bovine serum, 3% bovine calf serum, 5% penicillin streptomycin, 4 mM L-glutamine, 2.5 µg/ml fungizone and 0.1% insulin transferrin selenium, for 1 hr at 37°C, pipetting vigorously every 15 minutes;

centrifuging at 700 rpm for 3 minutes, resulting formation of a pellet and a first supernatant;

plating said first supernatant onto at least one 60 mm plating dish including growth media

2;

re-exposing said pellet to said collagenase A in said growth media 2, for 1 hr at 37°C,
pipetting vigorously every 15 minutes, resulting in formation of a second supernatant;

plating said second supernatant onto at least one 60 mm plating dish including growth media
2, for growth of a plurality of cells;

following approximately one month in said culture, and using a sterile pipette under sterile
conditions, gently scraping a plurality of cells from said dish and re-plating said cells onto at least one
60 mm plating dish including growth media 2, for growth of a plurality of cells;

after approximately 1 week in said culture, transferring a plurality of cells to at least one 100
mm plating dish including growth media 2, and maintaining said cells in said media until cells become
essentially confluent therein; and

approximately every 3 to 4 days, splitting the cells of said dish into fractions, then
transferring each fraction of same into one of a plurality (approximately 4) of plating dishes including
growth media 2, and maintaining said cells in said media until formation of additional cells, repeating
as many times as desired.

14. (Canceled) A method of identifying a compound that inhibits the activity of a protein kinase in
a cell, comprising the steps of:

providing a cell of claim 1 hereinabove,

contacting said cell with at least one inhibitor test compound, and

determining whether a protein kinase primarily localizes away from the cell membrane, said
localization being an indication that said test compound likely inhibits said protein kinase.

15. (Canceled) A method described in claim 14 hereinabove, wherein:

said protein kinase is an isoform known to be involved in hindering the organization of

cytoskeleton matrix in the cell cytoplasm, and

determining whether said isoform localizes primarily away from the cell membrane, said localization being an indication that said cell is apt to undergo organization of cytoskeleton matrix in the cell cytoplasm.

16. (Canceled) A method described in claim 15 hereinabove, wherein:

said protein kinase is PKC- α and said inhibitor test compound is retinoic acid, and determining whether PKC- α localizes primarily in a cytoplasmic and perinuclear region, said localization being an indication that said cell is apt to undergo organization of cytoskeleton matrix in the cell cytoplasm.

17. (Canceled) A method of determining the effect of a protein kinase inhibitor on a condition in a cell having manifestations consistent with cancer, comprising the steps of:

providing a cell of claim 1 hereinabove,

contacting said cell with at least one inhibitor of protein kinase known to be present in abnormally high levels in cells failing to undergo organization of cytoskeleton matrix in the cell cytoplasm, and

determining whether protein kinase primarily localizes away from the cell membrane, said localization being an indication that said cell is apt to undergo organization of cytoskeleton matrix in the cell cytoplasm.

18. (Canceled) A method described in claim 17 hereinabove, wherein:

said protein kinase is PKC- α and said inhibitor of protein kinase is retinoic acid, and determining whether PKC- α localizes primarily in a cytoplasmic and perinuclear region, said

localization being an indication that said cell is apt to undergo organization of cytoskeleton matrix in the cell cytoplasm.

19. (Canceled) A method, using a cell isolated *in vitro*, for predicting the effect on cell differentiation attributable to a differentiation enhancing test compound to be applied to an *in vivo* cancer cell, comprising the steps of:

providing a cell of claim 1 hereinabove,

contacting said cell with at least one enhancer test compound, and

determining whether actin filaments organize a cytoskeleton matrix, said organization being an indication that said test compound likely enhances cell differentiation.

20. (Canceled) A method as described in claim 19 hereinabove, wherein said enhancer test compound is retinoic acid.

21. (Currently amended) A hyperdiploid cellular composition comprising cells isolated from a poorly differentiated primary tumor of glandular epithelial cells of the endometrium of the uterus a ~~poorly differentiated human endometrial adenocarcinoma that is metastatic, said cells having characteristics consistent with primary tumor.~~

22. (Currently amended) A cellular composition as described in claim 21 hereinabove, wherein a plurality of said cells have at least an average of 48 chromosomes.

23. (Currently amended) A cellular composition as described in claim 22 hereinabove, wherein a

plurality of said cells are at least triploid at chromosome 3.

24. (Currently amended) A cellular composition as described in claim 22 hereinabove, wherein a plurality of said cells are at least triploid at chromosome 17.

25. (Currently amended) A cellular composition as described in claim 21 hereinabove, wherein a plurality of said cells have at least the following karyotypic characteristics: 48, XX, ?t (1:20) (p734.3; p11.2), dup (2) (q11.1q23), +3, del (5) (q723q731), ?add(6) (p23), add (7) (p721), +add (7) (q22), der(9;14) (q10;q10), add (15) (p11), +der (17) t(17;19) (p11.1;p11.1), 1 (19) (q10), ?del (20) (p711.2).

26. (Currently amended) A line of cells originating from a primary tumor specimen of poorly differentiated human endometrial adenocarcinoma ~~that is metastatic, said cells having characteristics consistent with primary tumor,~~ wherein a plurality of said cells differentiates in response ~~responds to~~ an anti-cancer compound in ~~substantially equivalent ways at the cellular level as said specimen.~~

27. (Currently amended) A line of cells as described in claim 26 hereinabove, wherein said anti-cancer compound comprises a protein kinase inhibitor ~~differentiating agent.~~

28. (Currently amended) A line of cells as described in claim 27 hereinabove, wherein said ~~differentiating agent~~ protein kinase inhibitor comprises a retinoic acid treatment.

29. (Previously added) A cellular composition as described in claim 26 hereinabove, wherein said cells are grown *in vitro* as a monolayer.

30. (Canceled) A cellular composition as described in claim 26 hereinabove, wherein said original specimen is superficially invasive.

31. (Withdrawn) A method of identifying a compound that inhibits the activity of a protein kinase in a cell, comprising the steps of:

- (a) providing a cell of claim 21 hereinabove,
- (b) contacting said cell with at least one inhibitor test compound, and
- (c) determining whether a protein kinase primarily localizes away from the cell membrane, said localization being an indication that said test compound likely inhibits said protein kinase.

32. (Withdrawn) A method described in claim 31 hereinabove, wherein:

- (a) said protein kinase is an isoform known to be involved in hindering the organization of cytoskeletal matrix in the cell cytoplasm, and
- (b) determining whether said isoform localizes primarily away from the cell membrane, said localization being an indication that said cell is apt to undergo organization of cytoskeletal matrix in the cell cytoplasm.

33. (Withdrawn) A method described in claim 32 hereinabove, wherein:

- (a) said protein kinase is PKC- α and said inhibitor test compound is a retinoic acid treatment, and
- (b) determining whether PKC- α localizes primarily in a cytoplasmic and perinuclear region, said localization being an indication that said cell is apt to undergo organization of cytoskeletal matrix in the cell cytoplasm.

34. (Withdrawn) A method of determining the effect of a protein kinase inhibitor on a condition in a cell having manifestations consistent with cancer, comprising the steps of:

- (a) providing a cell of claim 21 hereinabove,
- (b) contacting said cell with at least one inhibitor of protein kinase known to be present in abnormally high levels in cells failing to undergo organization of cytoskeletal matrix in the cell cytoplasm, and
- (c) determining whether protein kinase primarily localizes away from the cell membrane, said localization being an indication that said cell is apt to undergo organization of actin filaments into stress fibers in the cell cytoplasm.

35. (Withdrawn) A method described in claim 34 hereinabove, wherein:

- (a) said protein kinase is PKC- α and said inhibitor of protein kinase is a retinoic acid treatment, and
- (b) determining whether PKC- α localizes primarily in a cytoplasmic and perinuclear region, said localization being an indication that said cell is apt to undergo differentiation.

36. (Withdrawn) A method described in claim 35 hereinabove, wherein said organization of actin filaments into stress fibers in the cell cytoplasm indicates cell differentiation.

37. (Withdrawn) A method described in claim 35 hereinabove, wherein said differentiation comprises cell enlargement.

38. (Withdrawn) A method, using a cell isolated *in vitro*, for predicting the effect on cell differentiation attributable to a differentiation enhancing test compound to be applied to an *in vivo* cancer cell, comprising the steps of:

- (a) providing a cell of claim 21 hereinabove,
- (b) contacting said cell with at least one enhancer test compound, and
- (c) determining whether actin filaments organize into stress fibers cytoskeletal matrix.

39. (Withdrawn) A method as described in claim 38 hereinabove, wherein said enhancer test compound is a retinoic acid treatment.

40. (New) A cellular composition as described in claim 22 hereinabove, wherein a plurality of said cells are triploid at chromosome 7.

41. (New) A cellular composition as described in claim 21 hereinabove, wherein a plurality of said cells are triploid at chromosomes 3, 7 and 17 but only haploid at chromosome 14.

Application Title:	CELL LINE
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42. (New) A cellular composition as described in claim 21 hereinabove, containing 48 chromosomes, wherein a plurality of said cells are triploid at chromosomes 3, 7 and 17 but only haploid at chromosome 14.

43. (New) A human endometrial adenocarcinoma cell line designated CAC-1 having all of the identifying characteristics of CAC-1 cells.

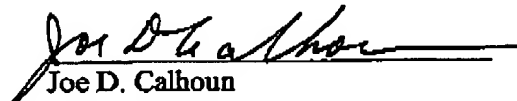
Application Title: CELL LINE
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III. CONCLUSION

Applicant believes that all deficiencies noted in the Notice of Non-compliant Amendment have been satisfied, the Response To Office Action Mailed 9/17/2003 fully satisfies all rejections and objections, and all remaining claims of this Application are in condition for allowance as a utility patent.

Respectfully submitted by:

CALHOUN LAW FIRM
P.O. Box 251504
Little Rock, AR 72225
501-374-1700
Telefax to 501-221-7058


Joe D. Calhoun
[Patent Bar Reg. # 40,293]

cc: Charleata A. Carter Ph.D.